

CASE: CT2777A US - CIP [1]  
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Remarks

Claim Amendments

Claim 1 was amended to remove reference to "solvates" and further amended to delete repetition of the term "-C<sub>1-3</sub>alkylene-" in the definition of Z.

Claim 21 deleted the phrase "wherein wherein" to "wherein".

Claim 29 deleted incorrectly transcribed references to the embodiments.

Claim 39 added reference to newly added claims 47-52.

Claims 47-50 are new and are directed to various embodiments provided for in the specification or to lists of compounds named or drawn in the specification.

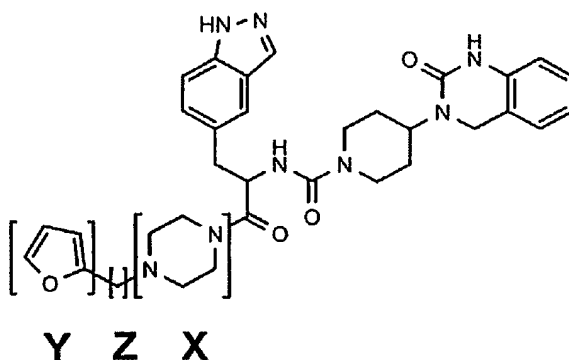
Claims 51 and 52 are directed to examples 47 and 48 respectively.

No new matter was added.

Indefiniteness of X and Y

Claim 1 and its dependent claims 2, 6-31, 37 and 39 were rejected as being indefinite because the definition of X and Y was deemed vague and unclear. Specifically, the Examiner raised three concerns: (1) use of the term "interrupted" when X and Y were both heterocycles (2) use of the term "and" to establish a conjunctive rather than a disjunctive relationship when describing optional features of X and Y and (3) the ability of X and Y to form a spirocyclic ring system. Applicants respectfully traverse the rejection and believe that the following explanations will address the Examiner's questions.

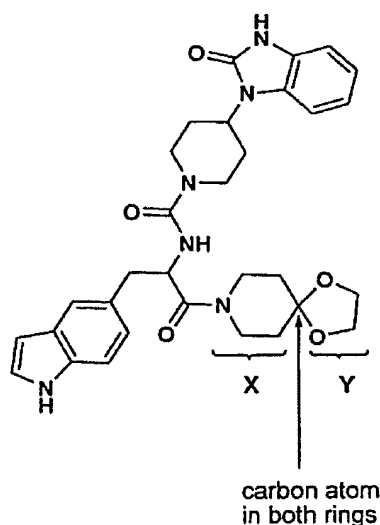
First, the Examiner is correct that X and Y can both be rings and that the claims permit them to be "optionally interrupted with Z," wherein Z is one of several "linking groups". Thus to "interrupt" X and Y means to insert something *between* X and Y and *not* necessarily something *into* X or Y. Example 40e illustrates the use of this definition as depicted below:

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As can be seen X is piperazinyl and Y is furanyl which are interrupted by Z which is a methylene ( $C_1$  of  $C_{1-3}$ alkylene).

Second, the claims permit X and Y to possess certain optional attributes. These options are linked by the term "and". Thus, the format of the claims permit X and Y to be (1) optionally interrupted; and (2) optionally substituted (3) optionally contain carbonyl(s). Because each feature is "optional", use of the conjunctive connector "and" instead of the disjunctive connector "or" leads to the same result, *i.e.*, X and Y may or may not be (1) interrupted (2) substituted or (3) contain carbonyl(s).

Third, X and Y may be joined to form a spirocyclic ring system. Since X and Y can be heterocycles, the Examiner queried (1) how the two heterocycles can be joined in a spirocyclic fashion and (2) whether the atom common to both rings can be nitrogen. Example 8 illustrates this aspect:



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As can be seen, X is piperidiny1 and Y is dioxolany1. They are two heterocycles joined in a spirocyclic fashion. In this example, the spirocyclic system shares a carbon atom. It is also possible for spirocyclic ring systems to share a nitrogen atom in which case the nitrogen atom will be positively charged.

Applicants respectfully submit that the foregoing explanations have addressed the Examiner's indefiniteness concerns and request that the rejection be withdrawn.

#### Indefiniteness of Claim 29

Claim 29 was rejected as being indefinite because it contained language referring to particular aspects and embodiments of the invention. Applicants have deleted this language which was a transcription error. Therefore, Applicants request that the indefiniteness rejection be withdrawn.

#### Non-enablement of Solvates

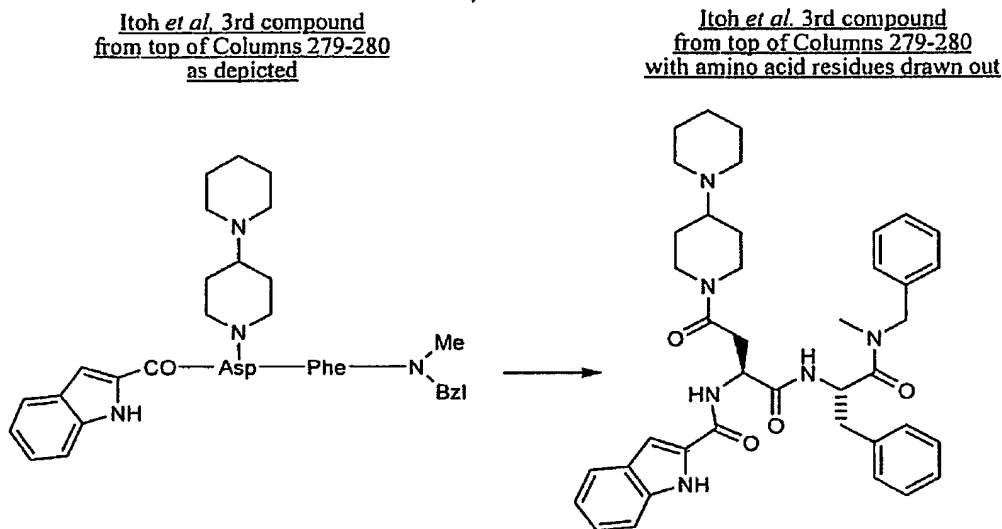
Claims 1, 2, 6-31, 37 and 39 were rejected under 35 U.S.C. 112, first paragraph, "because the specification, while being enabling for making pharmaceutically acceptable salts does not reasonably provide enablement for making solvate." In an effort to advance prosecution, Applicants have amended the claims to remove reference to solvates. Applicants therefore request that the rejection be withdrawn.

#### Obviousness in light of Itoh *et al.*

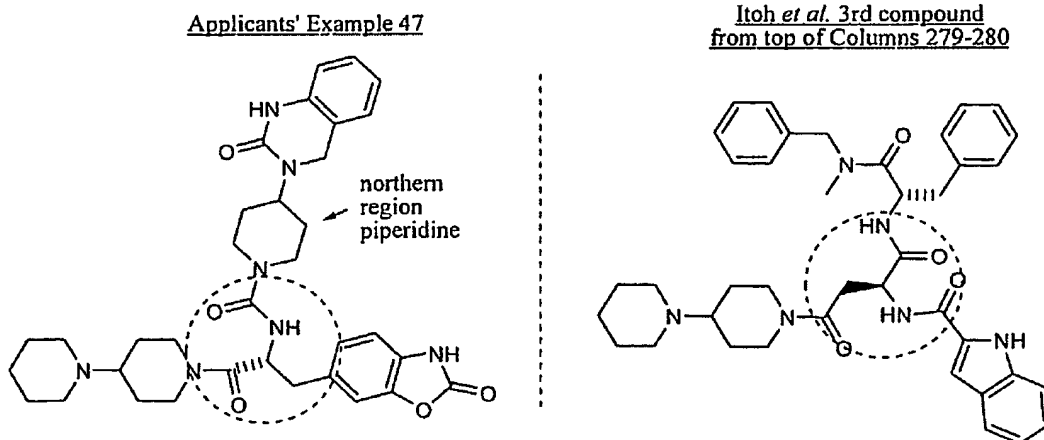
Claims 1, 6, 8, 13, 18, 20, 28-31 and 39 were rejected under §103 as being unpatentable over Itoh *et al.*, U.S. 5,932,737. Applicants respectfully traverse being that a *prima facie* case of obviousness has not been set forth. In order to establish a *prima facie* case of obviousness the prior art reference must teach or suggest with a reasonable expectation of success the claimed invention. The teaching and expectation of success must both be found in the prior art, not in Applicants' disclosure. See M.P.E.P. § 2143. The Examiner cited two examples from Itoh *et al.* and one generic substitution to support the obviousness rejection. Itoh is directed to inhibitors of nitric oxide whereas Applicants' compounds are CGRP receptor antagonists. Since no teaching or expectation of success was found in Itoh to lead one skilled in the art to Applicants'

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compounds, a *prima facie* case of obviousness cannot be supported. Neither Itoh example cited by the Examiner resembles the instant compounds. Nevertheless, Applicants have chosen to discuss Itoh's example that shared the piperidinylpiperidinyl substituent with Applicants. See Itoh *et al.* compound drawn third from the top in columns 279-280.



Applicants have reproduced the elected species Example 47 of the instant application for purposes of a comparison:



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As evident when the structures are drawn out, the compounds are structurally very dissimilar. One difference is the distinction of the backbones (as highlighted by the dashed circles). Applicants' backbone contains 5 atoms. Itoh's backbone contains *at least* 7 atoms. Moreover, the backbones of the two molecules exhibit marked differences in that Applicants' contains a urea whereas Itoh's contains amides. Thus, one skilled in the art of medicinal chemistry would expect the two compounds to adopt very different spatial conformations. The geometries of the molecules are further removed when considering the constrained nature of Applicants' piperidine ring in the northern region compared to Itoh's substituents in the northern region.

The third support for the obviousness rejection is not an example but a compound reconstructed by the Examiner from Itoh's general formula - specifically, where T is a piperidine. Applicants respectfully submit that this description does not create a structurally similar compound to those claimed even if such reconstruction were permitted. The Examiner also stated that,

"Itoh et al. differs from the instant claims in exemplifying only monocyclic heterocycle on the piperidine ring while instant claims require a fused bicyclic ring. However, Itoh et al. teaches equivalency of those compounds taught in column 33-490 with those generically recited in column 1-5. See R<sup>2</sup> definition and the definition of heterocyclic group which includes bicyclic rings."

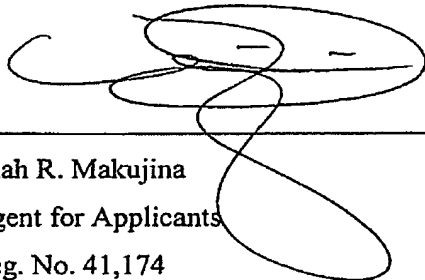
First, Applicants respectfully submit that Itoh differs in many more ways than the difference between a monocyclic and bicyclic ring system on the piperidine as described above. Second, Applicants have shown in the above example that the point of attachment of Applicants' piperidine in the northern region is not found in Itoh. Thus, Applicants respectfully submit that there is no teaching or suggestion in Itoh to arrive at Applicants' claimed compounds. Applicants therefore respectfully request that the obviousness rejection be withdrawn.

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In respect of the above, Applicants respectfully request the Examiner to enter said amendments and submit that the application is in condition for allowance. The Commissioner is authorized to withdraw any fees from Deposit Account 19-3880.

Respectfully submitted,

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Enclosure: Petition for Extension of Time